**AMENDMENTS TO THE SPECIFICATION**

Please replace paragraphs 0142 and 0153 with the following paragraphs.

**[0142]** To visualize the approximate ~~fimetional~~ functional relationships between protein kinases relative to the experimental data, kinases were hierarchically ordered based on their ability to phosphorylate the 12 different substrates (data available on the Internet at ~~web site~~ ~~http://~~bioinfo.mbb.yale.-edu/genome/yeast/chip as of Aug. 17, 2000). A profile corresponding to the -/+activity of the 107 protein kinases to each of the substrates was recorded, with discretized values in [0,1]. Matrices were derived from the pairwise Hamming distances between experimental profiles, and unrooted phylogenies were computed using the Fitch-Margoliash least-squares estimation method[45] as implemented in the FITCH program34 of the PHYLIP software package[44]. In each case, the input order of taxa was randomized to negate any inherent bias in the organization of the data set, and optimal hierarchies were obtained through global rearrangements of the tree structures.

**[0153]** To determine substrate specificity, the activity of a particular kinase was further normalized against the average of its activity against all substrates. Several examples are shown in FIG. 4b; all the data are available on the Internet at ~~http://~~bioinfo.mbb.yale.edu/genome/yeast/chip. Thirty-two kinases exhibited substrate specificity on a particular substrate with specificity index (SI; see Methods) equal or higher than 2, and reciprocally, most substrates are preferentially phosphorylated by a particular protein kinase or set of kinases. For example, the C terminus of Ax12, a protein involved in yeast cell budding, is preferentially phosphorylated by Dbf20, Kin2, Yak1 and Ste20 relative to other protein. Interestingly, previous studies found that Ste20 was localized at the tip of emerging buds similar to Axl2, and a ste20Δ/cla4$^{ts}$ mutant is unable to bud or form fully polarized actin patches or cables[28]. Another example is the phosphoprotein Gic2, which is also involved in

budding[16]. Ste20 and Skm1 strongly phosphorylate Gic2 (FIG. 4b). Previous studies suggested that Cdc42 interacts with Gic2, Cla4[29], Ste20 and Skm1. Our results raise the possibility that Cdc42 may function to promote the phosphorylation of Gic2 by recruiting Ste20 and/or Skm1.